Small-Cell Carcinoma of the Gallbladder: Report of a Case and Literature Review

Amit Mahipal, Shilpa Gupta
Thomas Jefferson University
Philadelphia, PA

Small-cell carcinoma (SCC) of the gallbladder is an uncommon, distinct clinicopathologic entity. It is an aggressive tumor that tends to metastasize early and is associated with a poor prognosis. It is also an extremely rare tumor, first described by Albores-Saavedra et al in 1981. Subsequently, numerous case reports have been published; however, a paucity of data on this tumor persists—to our knowledge, only 73 cases have been published in the English literature to date.[1–10] In this report we present the first case study of SCC of the gallbladder in an HIV-positive patient followed by a pertinent review of the English literature on this topic.

CASE REPORT

A 54-year-old woman with a history of HIV/AIDS presented with a 2–3 week history of right upper quadrant pain radiating to her back associated with nausea, dark urine, and jaundice. She had also lost 20 pounds over the last 3 months. Her medical history included HIV infection diagnosed 16 years previously, and she was noncompliant with antiretroviral therapy.

Physical examination revealed jaundice and right upper quadrant tenderness. Serum total bilirubin was 5.9 mg/dL, direct bilirubin 4 mg/dL, AST 277 U/L, ALT 378 U/L, and alkaline phosphatase 604 U/L. Ultrasound revealed a 7 × 5 cm mass replacing the gallbladder with periportal and peripancreatic lymphadenopathy. The mass was infiltrating the liver. Diffuse intrahepatic biliary duct and common biliary ductal dilation was also seen. Computed tomography (CT) confirmed the above findings, with no evidence of lung primary (Figure 1). Positron emission tomography (PET) scan showed avidity in 6.5 × 7 × 6 cm mass in the gallbladder and bilateral paraaortic, axillary, and iliac lymph nodes. Endoscopic retrograde cholangiopancreatography was performed, and a stent was placed to relieve common bile duct obstruction. Brush cytology showed atypical cells. Ultrasound-guided fine-needle aspiration cytology was performed that showed small, round cells with high nuclear-to-cytoplasmic ratio, which is consistent with high-grade small cell neuroendocrine carcinoma (Figure 2). Tumor cells were positive for chromogranin A, synaptophysin, and neuron-specific enolase.

Because of poor performance status and history of HIV, she was treated with single-agent carboplatin (area under the concentration-time curve [AUC] 5). She received three cycles of chemotherapy, interrupted by the onset of neutropenic fever. Unfortunately, repeat CT scan showed progressive disease with primary tumor increasing to 8.6 × 7.6 × 7.9 cm in size. She developed progressive jaundice due to multiple common bile duct and intrahepatic strictures unrelieved with biliary stent and died 14 weeks after diagnosis.

DISCUSSION

Small-cell carcinoma of the gallbladder is a rare disease, with Surveillance, Epidemiology, and End Results (SEER) data suggesting an incidence of approximately 0.5% of all gallbladder cancers.[11]

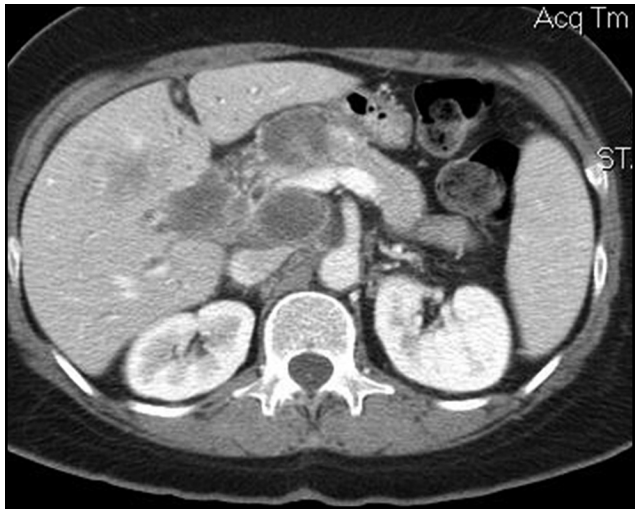

Figure 1. Computed tomography showing 7 × 5 cm gallbladder mass infiltrating the liver.

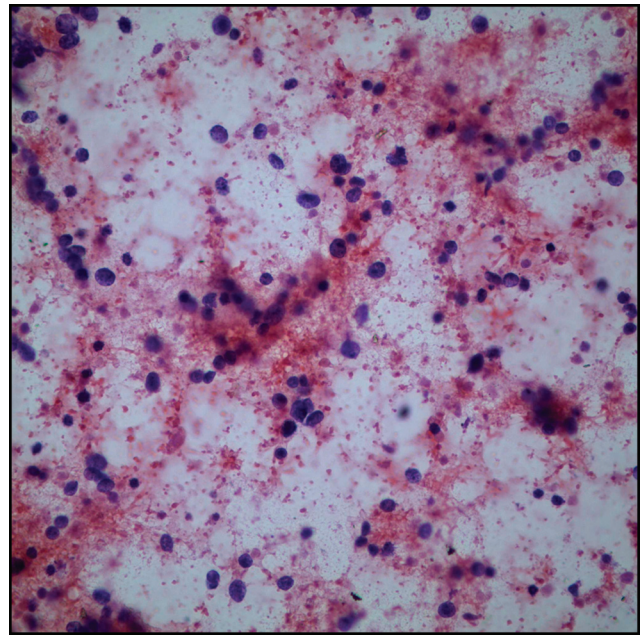

Figure 2. Fine needle aspiration cytology of the gallbladder showing small, round malignant cells consistent with small cell carcinoma.

Table 1. Characteristics of patients with small-cell carcinoma of gallbladder*

Number of patients	74
Clinical cases	55
Autopsy cases	19
Median age (range) in years (n = 73)	67 (25–86)
Sex (n = 74)	
Men	25 (34%)
Women	49 (66%)
Histology (n = 57)	
Pure small-cell carcinoma	41 (72%)
Combined	16 (28%)
Cholelithiasis (n = 73)	50 (68%)
Stage (n = 71)	
I–III	24 (34%)
IV	47 (66%)
Metastases	
Lymph nodes (n = 71)	50 (70%)
Liver (n = 70)	45 (64%)
Lung (n = 70)	7 (10%)
Surgery (n = 43)	40 (93%)
Chemotherapy (n = 43)	20 (47%)
Median survival (range) in months	9 (1–189)

*n = number of patients for whom data were available for the particular characteristic.

Moskal et al in their series reported a higher incidence of 3.5%.[7] Only 73 cases have been reported in the literature, out of which, 54 were clinical cases and 19 were autopsy cases. Table 1 lists the characteristics of the reported cases, including our case.

Median age is 67 years, ranging from 25–86 years. It shows a higher predilection for women, who account for 66% of cases. Cholelithiasis was found in 68% of cases. It is not known at this time whether this is just an incidental finding or a clinically significant association exists. Histology showed 72% (n = 41) as pure SCC and 28% (n = 16) as combined SCC and adenocarcinoma or squamous cell carcinoma. The prognostic significance of pathologic subtypes of SCC remains undefined. The data suggest similar survival between the pure and combined subtypes. Forty-seven out of 71 (66%) were diagnosed at stage IV and 24 at stages I to III. The most common site of metastases was lymph nodes (70%), followed by liver (64%), and lungs (10%).

Surgery was performed in 93% (40 of 43) of cases. Of 43 patients, 20 (47%) received chemotherapy. Cisplatin and etoposide was the most common regimen used followed by 5-florouracil. Median survival was only 9 months, ranging from 1 to 189 months. Chemotherapy was associated with better survival, with a median survival of 13 months vs. 4 months in patients who received no chemotherapy ($p < .05$).

The prognosis of SCC of the gallbladder remains poor, with the majority of patients presenting with metastases. It is hoped that with advances in multimodality therapy the prognosis will improve. Accordingly, prospective trials designed to define the best therapy for this disease is are clearly needed.

REFERENCES

1. Albores-Saavedra J, Cruz-Ortiz H, Alcantara-Vazques A, et al: Unusual types of gallbladder carcinoma. A report of 16 cases. *Arch Pathol Lab Med* 105:287–293, 1981
2. Bahadur S, Shaukat A, Gibbs J, et al: Cisplatin and gemcitabine for small cell carcinoma of the gall bladder. *Am J Clin Oncol* 28:425–426, 2005
3. Fujii H, Aotake T, Horiuchi T, et al: Small cell carcinoma of the gallbladder: a case report and review of 53 cases in the literature. *Hepatogastroenterology* 48:1588–1593, 2001
4. Imai H, Matsui S, Tokuyama Y, et al: Small cell carcinoma of the gallbladder successfully treated by surgery and adjuvant chemotherapy. *Am Surg* 74: 272–273, 2008
5. Maitra A, Tascilar M, Hruban RH, et al: Small cell carcinoma of the gallbladder: A clinicopathologic, immunohistochemical, and molecular pathology study of 12 cases. *Am J Surg Pathol* 25:595–601, 2001
6. Matsuo S, Shinozaki T, Yamaguchi S, et al: Small-cell carcinoma of the gallbladder: report of a case. *Surg Today* 30:89–93, 2000
7. Moskal TL, Zhang PJ, Nava HR: Small cell carcinoma of the gallbladder. *J Surg Oncol* 70:54–59, 1999
8. Pavithran K, Doval DC, Vaid AK, et al: Small cell carcinoma of the gall bladder: case report and review of literature. *Trop Gastroenterol* 22:170–171, 2001
9. Piana S, Cavazza A, Corrado S, et al: Combined small cell carcinoma and clear cell carcinoma of the gallbladder: report of a case and review of the literature. *Pathol Res Pract* 198:821–824, 2002
10. Uribe-Uribe NO, Jimenez-Garduno AM, Henson DE, et al: Paraneoplastic sensory neuropathy associated with small cell carcinoma of the gallbladder. *Ann Diagn Pathol* 13:124–126, 2009
11. Henson DE, Albores-Saavedra J, Corle D: Carcinoma of the gallbladder: histologic types, stage of disease, grade, and survival rates. *Cancer* 70:1493–1497, 1992

Disclosures of Potential Conflicts of Interest

The authors indicated no potential conflicts of interest.

Address correspondence to: Amit Mahipal MD, MPH, Thomas Jefferson University, 834 Chestnut Street, Suite 320, Philadelphia PA 19107. Telephone: (612) 298-5401; Fax: (215)955-9641; E-mail: amitmahipal@gmail.com